

Self-perceptions of speech, voice, and swallowing in motor phenotypes of Parkinson's disease

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ABSTRACT

Introduction: The ability of people with Parkinson's Disease (PWP) to perceive and identify impairments related to communication and swallowing is often impaired. This impairment prolongs the time to diagnosis of dysphonia and dysphagia, and can delay implementation of speech or swallowing therapy. We have limited knowledge of how different motor phenotypes of PD impact speech, voice and swallowing, nor how PWP perceive these impacts. The purpose of this study was to identify how perceptions of speech and voice impairments predict dysphagia in PD, and how those perceptions differ between motor phenotypes.

Methods: 38 PWP completed clinical surveys including V-RQOL, DHI, and a speech, voice, and swallow symptom questionnaire. Participants were categorized as either tremor dominant (TD) or non-tremor dominant (NTD) phenotypes. Multiple regression and MANOVA were utilized to identify predictors of dysphagia perceptions, and for differentiating between motor phenotype based on perceptual severity.

Results: Perceptions of speech and voice impairment predicted perceptions of swallow impairment regardless of phenotype ($p < .05$, $CI = 0.08-0.77$). NTD participants reported significantly more communication and swallowing impairments than TD ($p < .05$) and perceived communication impairment severity was the strongest predictor of group classification ($OR = 0.50$). The survey battery displayed a robust discriminatory ability between phenotype ($AUC = 0.87$, $CI = 0.76-0.98$).

Conclusion: The use of a noninvasive and cost-efficient survey battery may be useful in predicting patient perceived swallow impairment in PWP. Speech, voice, and swallow impairments based on survey responses were found to differ between motor phenotypes.

1. Introduction

Impairments of speech and swallowing are expected to occur at rates as high as 95% in people with Parkinson's Disease (PWP) across the full time-course of the disease [1,2]. It is likely that a combination of sensorimotor and executive function deficits contribute to these impairments [3,4]. The ability of PWP to perceive the presence and severity of these speech and swallowing impairments appears to also be impaired. Multiple studies have shown an inability of PWP to perceive or self-correct speech deficits [5,6] and a decreased ability to perceive swallow deficits [7].

A limited number of studies have shown that the ability of PWP to perceive changes in speech and/or swallowing is impacted even in the non-advanced stages of disease progression. Available research has shown that communication deficits occur early and are some of the most salient impairments in PWP regardless of disease stage or duration [8]. In one study more than 40% of PWP identified changes in swallow function, which were shown to be associated with penetration and/or aspiration. This

same study also highlighted the concurrence of reported speech and voice impairments with swallow impairment [9].

There is also limited knowledge of how the heterogeneous nature of PD influences the progression and severity of speech and swallowing impairments. For example, it is not clear how different forms of PD motor phenotype (i.e., tremor vs. non-tremor dominant) impact the manifestation of communication impairments in PWP, or how motor phenotype affects the ability to perceive those impairments [10]. Patient based reports of communication deficits from PWP have shown Non-Tremor Dominant (NTD) PWP reported greater communication impairment than Tremor Dominant (TD) [11,12]. However, physiological evidence of speech and voice function in PWP as a function of phenotype have shown conflicting results [8,13].

There is also limited knowledge of how dysphagia manifests in different PD phenotypes or how dysphagia progresses from the time of PD diagnosis [14]. This has led to poor understanding of the degree of swallow impairment experienced by PWP in non-advanced stages, and if they are able to predict existing swallowing impairments. Dysphagia in non-advanced PD may not be perceived without overt signs or symptoms, while oral-motor and/or speech deficits may be more pronounced [15] and therefore more readily diagnosed than impaired swallow function. There is an apparent gap in our knowledge associated with the perceptual and physiological

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characteristics of swallowing impairment related to both non-advanced stages of PD and different PD phenotypes.

The current study sought to answer three questions. The first question asked: How do PWPD perceive speech, voice, and swallowing impairments and how well do their perceptions of speech and voice predict their awareness of swallowing impairments. We hypothesized that PWPD, when provided with a perceptual questionnaire specific to swallowing symptoms, would be able to identify symptoms of swallowing impairment. We then hypothesized that those perceptions would be predicted by similar perceptions in the domains of speech and voice (communication) function. That is, as the frequency of perceived speech and voice impairment symptoms increases, so would the frequency of perceived swallow impairments. The second question asked if there were differences in speech or swallow impairment perceptions between tremor dominant (TD) and non-tremor dominant (NTD) phenotypes. We hypothesized that NTD would report a greater frequency of symptoms in at least one domain of speech or swallowing. The final question asked how accurately perceptions of speech and swallowing impairment could predict whether an individual with PD was tremor or non-tremor dominant. We hypothesized that the perceptual reports of speech and swallowing impairment would accurately classify PWPD of different phenotypes.

2. Methodology

38 PWPD were recruited as part of an ongoing program of research. Inclusion criteria consisted of: 1) a diagnosis of idiopathic PD by a neurologist, 2) current disease severity in stage I-III based on Hoehn and Yahr (H&Y) score, and 3) no comorbid neurological impairments associated with conditions other than PD. Information relevant to disease history, stage and progression was collected including gender, age at diagnosis, years post diagnosis, Hoehn and Yahr stage (H&Y), and tremor phenotype. Tremor phenotype determination has been described and performed in previous work from our lab [13], therefore the PI's assigned participants to either TD or NTD based on a combination of factors including neurologist report, patient history, and patient responses to a motor questionnaire (Appendix A). There is conflicting evidence on the best approach to determining motor-based phenotypes of PD. Some previous communication and swallowing literature have utilized a cutoff score derived solely from motor severity scales such as the Unified Parkinson's Disease Rating Scale (UPDRS) [14,16]. However, more recent work has suggested this standard of determining motor or tremor phenotyping lends to significant variability and unreliable phenotyping upon reexamination [17]. We therefore chose to use a stratification strategy for tremor phenotype similar to that of Selikhova et al. [18] and has been used previously in the literature [13]. Participants were categorized as TD phenotype if they met the following criteria: (a) a unilateral tremor was the predominant initial sign of the disease, (b) there was a report and clinical confirmation of tremor progression since initial diagnosis, and (c) tremor was a current major sign and impairment associated with PD in relation to other motor signs. Participants were categorized as NTD phenotype if they met the following criteria: (a) There were no reports of tremor at initial onset, (b) there was a report and clinical confirmation of minimal progression of tremor since diagnosis, and (c) tremor was not a current major manifestation or impairment associated with PD. Based on this dichotomous categorization, any participant who did not meet criteria for TD phenotype was assigned to the NTD group. After consenting procedures, participants completed a battery of self-perception assessments and questionnaires. This included the Dysphagia Handicap Index (DHI) [19] and the Voice Related Quality of Life (V-RQOL) [20].

A custom questionnaire for the self-report of speech and voice (communication) and swallow impairment symptoms was also administered (see Appendix A). The goal of the questionnaire was to establish an overall count of communication and swallowing symptoms perceived by the participants. While both the DHI and V-RQOL have subdomains of their questionnaires and different overall scoring techniques [19,20], both utilize an overall severity score. Therefore, rather than have each item be counted separately in our questionnaire, items related to speech and voice were

totalled to determine a communication severity score, and the same was done with all swallowing questions to determine a swallow severity score. The questionnaire asked participants to rate their perceptions of speech, voice, and swallowing symptoms during a typical day, when their impairments from PD would be at their worst. Participants rated each symptom as "Never", "Occasionally", "Sometimes", "Often", or "Always". For each item that participants rated as occurring more often than never, 1 point was recorded. Each item was scored 1 as the goal of the questionnaire was not to determine the severity of each item, but to establish a total count of symptoms being perceived in each domain (communication and swallowing). As an example, there are 8 total swallow symptom questions ranging from "Drooling" to "Food or pills gets stuck in throat". If a participant confirmed they experienced all of these problems at least occasionally, they would be scored 8 on the swallow symptom count. A higher count of symptoms would therefore indicate a higher level of symptom severity being experienced by the participant. This method was applied to all symptom sections of the questionnaire, including swallowing symptoms and communication symptoms. All questionnaires were completed by the participants, independently and one at a time, in the presence of one of the PIs. When each questionnaire was completed the scores were tallied and recorded by the PI.

Statistical analyses were performed in SPSS (v. 24). Descriptive statistics and frequency tables were computed to identify target demographic information including motor phenotype, age at diagnosis, years post diagnosis, H&Y staging, and scores from questionnaires. A standard multiple linear regression (MLR) was run to determine the ability of self-reported perceptions of speech & voice symptoms and V-RQOL to predict increased frequencies of swallow symptoms on a custom questionnaire. We utilized a standard entry method with all variables of interest entered into the model, rather than a stepwise regression method, in order to minimize type I error. The DHI was not included into our regression model due to the anticipated likelihood of extreme influence on model results, as the DHI and the swallow symptom perceptions are likely to measure similar symptomology.

A multivariate analysis of variance (MANOVA) was used to determine differences in communication and swallowing symptom frequency counts (speech & voice symptoms, V-RQOL, DHI, and swallow symptoms) reported between TD and NTD phenotypes. Finally, a multivariate binomial logistic regression (LR) was performed to predict group membership of phenotype by the independent variables of speech & voice symptoms, V-RQOL, DHI, and swallow symptoms. We then used the predicted probabilities derived from the logistic regression (PRE_1) in a ROC analysis to evaluate the regression model's ability to discriminate between TD and NTD phenotypes, based on the risk of reporting scores of communication and swallow impairment perception. All α levels for rejecting the null were set to 0.05.

3. Results

Descriptive statistics including mean, median, and standard deviation, of the participant sample are included in Table 1. All variables and descriptive statistics fell within appropriate skewness (<2) and kurtosis (<7), therefore indicating a normal distribution in our data to proceed with hypothesis testing. 38 participants ($n = 38$) were included with no participants excluded from final analysis and no missing data points. Participants had a mean age of 66 and mean time post diagnosis of 3.9 years. 24 (63%) participants were classified as NTD, with the remaining 14 (37%) classified as TD. H&Y staging (median & interquartile range) for TD was 2.5(1) and 3(0.75) for NTD. Bivariate analysis using independent samples *t*-tests indicated no significant differences of demographic information between TD and NTD including age at time of investigation, age at diagnosis, and years post diagnosis. Chi-Square tests similarly displayed no differences in gender distribution or H&Y stages between TD and NTD. Cumulatively, 71% of participants reported a DHI score >7 , and 53% of participants reported a swallow symptom frequency of ≥ 3 symptoms. 71% reported a speech & voice symptom frequency ≥ 3 , and 100% of participants reported a total V-RQOL score of <50 .

Table 1
Descriptive Statistics of TD and NTD phenotype PWPDP.

Participant characteristics	Tremor dominant Mean (\pm SD); median	Non-tremor dominant Mean (\pm SD); median
Hoehn and Yahr ^a	2.5(1)	3(0.75)
Gender distribution (% male/female)	57%/43%	63%/37%
Age at diagnosis	64.4(9.7); 66.5	67(7.8); 68
Years post diagnosis	3.9(2.5); 3.2	3.8(3.1); 2.9
Age at time of investigation	68.3(9.1); 71.3	70.9(6.5); 6.5
Speech & voice severity	2.3(1.7); 2	4.6(1.5); 5
Swallow severity rating	1.8(1.5); 2	3.3(1.9); 3
DHI	10.8(11.5); 7.5	13.1(9.7); 10
V-RQOL	14.2(5.2); 15	21.3(10); 20

^a Expressed as median (interquartile range).

The regression met all necessary assumptions including linearity, tolerance (>0.2), VIF (<10), & all correlations were well below threshold (>0.7). Our regression model produced a significant result ($F[35] = 8.13$, $p = .001$), with an adjusted $R^2 = 0.28$, indicating the variables present in our model were accounting for 28% of the variance in our data. For predicting the perception of swallowing impairment overall, participants' perceptions of speech and voice symptoms were the strongest predictor in the model ($\beta = 0.43$, $p = .017$, $CI = 0.08-0.77$). V-RQOL did not significantly contribute to predicting perceptions of swallowing impairment. An overall model and coefficient summary are presented in Table 2.

Our MANOVA met all necessary assumptions including linearity inspection of scatterplots, skewness/kurtosis measures of normality within acceptable ranges (<2 and <7), and Box's Test of Equal Variances >0.001 . There were no outliers excluded from analysis. The overall multivariate model displayed a significant result ($\Lambda = 0.605$, $F[4, 33] = 5.397$, $p = .002$), indicating the leveraged results of dependent variables in the model displayed a significant effect of phenotype on communication and swallowing symptom reporting in our sample. An analysis of our Tests of Between Subjects Effects indicated that speech and voice symptoms ($F = 18.95$, $p < .001$), swallowing impairment symptoms ($F = 6.48$, $p = .02$), and V-RQOL ($F = 6.01$, $p = .02$) were all significantly worse in the NTD group compared to the TD. There was no effect of phenotype for DHI reporting, despite differences in mean reporting score. A model summary with effect sizes are presented in Table 3.

The LR model revealed a significant result above the constant model ($\chi^2 [4] = 17.6$, $p = .001$), and the Hosmer & Lemeshow Test of model fit ($\chi^2 = 3.21$, $p = .921$) indicated that our predictive model accurately fit the observations within our data. Analysis of the predictor variables contribution to the model showed speech and voice symptoms as the strongest contributor ($\beta = -0.70$, $W = 3.92$, $p = .048$, $OR = 0.50$). The odds ratio (OR) for speech and voice symptoms ($OR = 0.50$) indicated that TD phenotype PWPDP displayed a 50% decrease in the odds of reporting increased speech and voice symptoms. No other predictor variables contributed significantly to the model for predicting phenotype group. Despite the non-significant results, counts of swallow symptoms ($OR = 0.63$) indicated that TD phenotype displayed a 37% decrease in the odds of reporting increased swallow symptoms. The DHI and V-RQOL did not contribute significantly to predicting group membership ($p > .05$) and provided minimal change in the odds of being classified into either group ($OR = 1.1$ and 0.95 , respectively). A comprehensive model summary is provided in Table 4.

Our subsequent ROC analysis for determining the sensitivity or specificity of the use of questionnaires to predict whether an individual belonged to the TD or NTD phenotype groups (Fig. 1) revealed a significant result and positive area under the curve for the combined predicted probabilities of

Table 2
Linear regression for predicting reported swallow symptoms: model and coefficient summary.

Perceptual predictors	β	Std. β	Sig. (p-value)	CI (95%)
Speech and voice severity rating	0.43	0.42	0.017	0.08–0.77
V-RQOL	0.04	0.21	0.23	–0.03–0.12

Table 3
Multivariate analysis of communication and swallowing perceptions between NTD and TD.

Perceptual variables	F statistic	Sig. (p-value)	Pairwise difference (NTD-TD)	Effect size (A1) ω^2
Speech and voice severity rating	18.95	<0.001	–2.30	0.07
Swallow severity rating	6.48	0.02	–1.55	0.04
V-RQOL	6.01	0.02	–7.08	0.02
DHI	0.45	0.51	–2.34	0.006

0.87 ($p < .001$, 95% $CI = 0.76-0.98$). This suggested that the utilization and scoring of tools used in this study for perceptions of speech & voice symptoms, swallow symptoms, and V-RQOL were robust for discriminating between TD and NTD phenotype in PWPDP.

4. Discussion

4.1. Perceptual Reporting of Communication and Swallowing in PWPDP

The goals of this study were to investigate perceptions of speech, voice and swallowing in PWPDP as well as identify relevant differences in symptomatic perceptions between two motor phenotypes of PWPDP. Our results indicated that the sample of PWPDP in our study, all of whom were in non-advanced stages, were able to identify speech, voice, and swallowing symptomology regardless of motor phenotype. Communication and swallowing changes such as those perceived by participants in this study have been documented to negatively affect overall quality of life in PWPDP [21,22]. Results from this study are not in agreement with previous reports, which have indicated that PWPDP demonstrated an impaired ability to consistently perceive and identify communication and swallow impairment. Rationale for that impairment was associated with changes to both central and peripheral sensorimotor feedback loops [23,24]. However, we found that a set of questionnaires with questions specific to communication (speech and voice) and swallowing function increased the likelihood that participants would be able to identify impairments

Our theory as to why participants in this study were able to perceive swallowing impairment symptoms is that we provided them with specific questions that allowed for intentional consideration of multiple perceptual factors specific to speech, voice and swallowing. It is possible that using multidimensional perceptual prompts for symptomology increases the participant's odds of identifying communication or swallowing impairment. This would typically be a concern when interpreting regression results. However, our results indicated that all perceptual measures were well below the accepted correlation threshold. This suggested that while our questionnaire battery may be addressing similar constructs, administering them together increases the likelihood of a patient reporting impairment. Similarly, the DHI and V-RQOL have reported good test-retest reliability (0.83 and 0.93, respectively) even in populations with neurological impairment, including PD [19,20]. Recent work has also suggested that when provided with specific questions related to swallow function, a questionnaire may be able to predict impaired swallow function in people with PD [25]. This supports the notion that while we are asking different communication and swallowing symptom questions, the construct of the questions being asked may be stable enough to include in a battery of perceptual questionnaires to help detect communication or swallow impairment.

The results from our present cohort also indicated that reports of speech and voice impairments may predict the reporting of swallowing impairment. Van Hooren et al. [26] have previously reported that a decline in voice related quality of life is associated with a decline in swallowing related quality of life, consistent with our findings. Though the questions in their work were different from ours, their use of questionnaires was similar to the one used in this study in administering multiple questionnaires of communication and swallowing was performed to observe differences in perceived impairment between groups. Our results build on this body of literature, indicating that the frequency of speech and voice symptoms

Table 4
Logistic regression model for predicting phenotype group.

Perceptual classifiers	β	Wald statistic	Sig. (p-value)	OR (95%CI)
Speech and voice severity rating	-0.703	3.9	0.04	0.50 (0.25–0.99)
Swallow severity rating	-0.46	1.6	0.20	0.63 (0.31–1.3)
DHI	0.10	2.1	0.15	1.1 (0.96–1.3)
V-RQOL	-0.06	0.48	0.49	0.95 (0.81–1.1)

reported may be used to predict an increased risk of swallowing impairment in PWP. These findings may be applicable in clinical settings as diagnosed speech or voice impairment may indicate the need to further assess swallowing function.

4.2. Differences in Communication and Swallowing Perceptions by Motor Phenotype

Previous studies have shown that motor phenotype influenced the severity of disease manifestation and differences in disease progression [27], in addition to decreased quality of life perception [28]. Results from this study indicated that PWP categorized as NTD were likely to report symptoms of impairment more frequently than the TD group. Those categorized as NTD reported significantly more frequent or severe communication and swallowing impairments across all assessments except for the DHI. In terms of classifying people with PD into TD or NTD phenotype based on communication or swallowing impairment reports, communication impairment severity was the most important contributing factor ($p = .048$, OR = 0.50). Recent physiological outcomes by Tykalová et al. [29] lend support to these findings, as their results indicated communication impairment was a significant discriminating factor between TD and NTD, and impairment was more severe in NTD subjects. In addition, while non-significant, reports of more severe swallow symptoms were reported substantially less in TD than in NTD (OR = 0.63). This may indicate that while the overall severity of the symptoms themselves may not be perceived as more or less severe, people with PD may report experiencing more symptoms overall. The approach of allowing people with PD to identify specific communication or swallowing symptoms on the basis of the number of symptoms being reported rather than how severe the symptoms are may increase identification of communication or swallowing impairment and therefore, referral for assessment. Although addressing different outcomes, Andres et al. [30] found that even though PWP may not meet a pre-specified

total cutoff score on a questionnaire to be considered as possibly having dysphagia, they may report multiple symptoms without reporting a high severity of the symptoms. More than 93% of individuals who reported at least some type of dysphagia were confirmed to have impaired swallow safety or efficiency after assessment.

The combined use of these perceptual assessments was also able to discriminate the risk of increased communication and swallowing impairment based on participant perception between the two tremor phenotypes of PD in this study. These findings may have direct clinical implications. The NTD motor phenotype in PWP has been associated with more rapid and more severe disease progression, faster deterioration of both motor and non-motor domains, and decreased quality of life outlook compared to the TD phenotype [31]. Therefore, the ability to use inexpensive and quick assessment methods such as questionnaires to identify who may be at increased risk of communication and swallow impairment may be beneficial in developing a therapeutic prognosis.

There is still mixed evidence in the PD literature about the validity of using a TD vs. NTD classification scheme to predict long-term outcomes due to the heterogenous nature of the disease [32]. Despite the multifactorial and heterogenous nature of PD, the benefits of classifying motor phenotype in a noninvasive and cost-efficient manner for targeted treatments and anticipating symptom progression may still be beneficial [33] to healthcare providers that serve PWP. The results from our study indicate that the use of a battery of perceptual assessments related to speech, voice and swallowing may discriminate motor phenotypes in PD successfully in those at non-advanced stages. This presents an efficient, cost effective, and noninvasive approach to phenotyping PWP for clinical considerations. Future research regarding perceptions of impairment related to communication and swallowing should focus on corroborating physiological distinctions between motor phenotypes with perceptual measures to determine the level of actual physiological impairment, rather than only perception.

4.3. Limitations

There are several limitations of the present study which warrant caution when considering generalization of findings. A major aim of the study was to identify self-reported perceptual levels of impairment by PWP. Therefore, no physiological data was included to confirm the presence of swallowing, speech, or voice impairments at the time of data collection. This is important to note as subjects may have perceived subtle or sub-clinical fluctuations in communication or swallow function and therefore would not be diagnosed on clinical examination by a speech-language pathologist. Additionally, the custom questionnaire used within this study has not been validated or tested for reliability, and construct validity has not been assessed to date. Therefore, isolated conclusions from the results of the custom questionnaire should be used cautiously. While our results indicate that a battery of testing may help identify communication and/or swallow impairment and possibly discriminate between tremor phenotypes, the use of this custom questionnaire as a clinical tool requires substantially more examination as a standalone assessment. The group sample sizes and demographics of the total cohort were only 24 (NTD) and 14 (TD). It is possible that the uneven sample sizes favored NTD, who reported more severe impairment perceptions. A larger sample may reveal similar severity trends in perceptual measures in TD phenotypes, which future research will need to address. Similarly, this sample used in this study was a small cohort (38) from a specific geographical area, which may not be representative of the larger population of PWP globally.

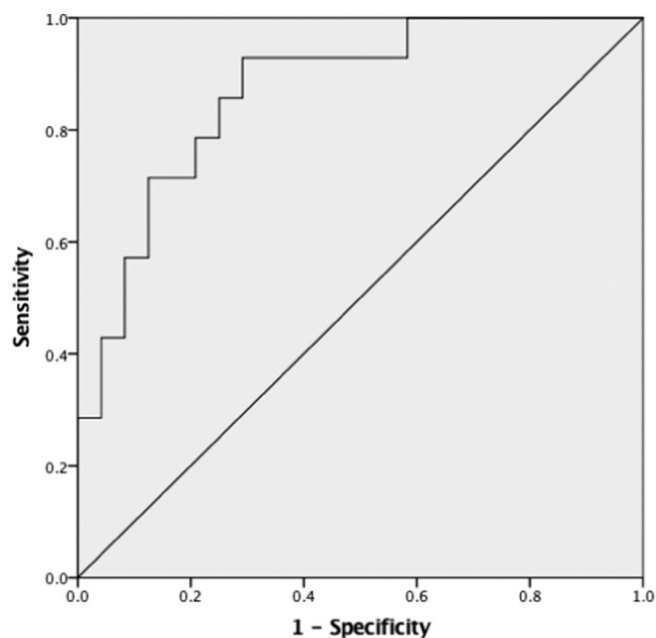


Fig. 1. AUC graph for discriminating phenotype membership by communication and swallow impairment measures.

There was also no control group included in the conduction of this study. Therefore, while the participants in this study report increased communication and swallow impairments we are unable to conclude if these impairments are different from healthy older adults of a similar age. However, normative data from healthy controls for the V-RQOL indicate that scores even as low as 80 indicate a good perception of their voice quality. Our results for both groups indicate significant deviations from this threshold. The DHI indicates controls are expected to have a mean total score of approximately 2. Similar to the V-RQOL, our results indicate a substantial deviation from what is expected in control subjects. However, in order to draw more precise conclusions from this information, future directions of this research should be to include control subjects to observe differences. In addition, the PIs were not blinded to the assignment of participants to either TD or NTD groups. While not a goal of this study to determine the clinical utility of how participants were assigned to phenotype, this introduces an inherent level of bias into the study design. This may have influenced or introduced an increased level of error in group stratification, and should therefore be interpreted with great caution when considering differences between phenotype.

CRedit authorship contribution statement

Both authors (Matthew Dumican & Christopher Watts) contributed equally and appropriately to the curation of this manuscript. All aspects of project execution and manuscript preparation were performed and completed in consultation with the other author. This includes: conceptualization, methodology, data curation and analysis, writing and editing of the manuscript, and overall project administration and completion.

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Declaration of competing interest

None.

Appendix A. Speech, voice and swallow severity ratings

Parkinson’s Speech, Voice, Swallowing, and Motor Questionnaire

Answer the following based on what you experience during a typical day when your symptoms are at their worst

Do you experience any of the following?

Problem	Never	Occasionally	Sometimes	Often	Always
Speaking volume is low					
Voice sounds hoarse					
Pitch does not vary when speaking					
Articulation is slurred or mumbled					
Speech rate is too fast					
Speech rate is too slow					
Air comes out of nose when speaking					
Drooling					
Food falls out of mouth when eating					
Food gets stuck in cheeks when eating					
Clear throat frequently when drinking					
Clear throat frequently when eating					
Cough frequently when drinking					
Cough frequently when eating					
Food or pills gets stuck in throat					
Tremor in hand					
Tremor in arm					
Tremor in foot					
Tremor in leg					
Tremor in head or neck					
Tremor in face or tongue					
Movements are slow					
Muscles are stiff					
Balance problems					
Falling over					
Difficulty getting up from chair					
Posture is slumped when standing					
Shuffling feet when walking					

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